Claims

WHAT IS CLAIMED IS:

1. A composition for use in delivering a bioactive agent to targeted tissues or cells comprising:

(a) a site-specific targeting ligand;

(b) a lipid encapsulated oil in water emulsion; and

(c) a bioactive agent in or on the surface of the outer monolayer said emulsion; said ligand being conjugated directly or indirectly to said emulsion and said composition providing facilitated delivery of said bioactive agent through prolonged association and increased contact of the ligand-bound, lipid encapsulated emulsion particles with the lipid bilayer of said target tissues or cells.

2. A composition as set forth in claim 1 wherein said site-specific targeting ligand is selected from the group consisting of antibodies, antibody fragments, peptides, asialoglycoproteins, polysaccharides, aptamers, small molecules, nucleic acids, peptidomimetics, mimetics and drugs.

3. A composition as set forth in claim 2 wherein said site-specific targeting ligand is an antibody.

4. A composition as set forth in claim 1 wherein said oil in water emulsion contains a fluorochemical.

5. A composition as set forth in claim 4 wherein said fluorochemical is a fluorocarbon.

6. A composition as set forth in claim 4 wherein said fluorocarbon is perfluorooctylbromide.

7. A composition as set forth in claim 4 wherein said fluorochemical is a liquid with a boiling point above approximately 30°C.

8. A composition as set forth in claim 7 wherein said fluorochemical liquid has a boiling point above approximately 90°C.

9. A composition as set forth in claim 1 wherein said bioactive agent is selected from the group consisting of chemotherapeutic agents, drugs, genetic materials, nucleic acid-based therapy, protein or peptide therapy, radioactive isotopes or combinations thereof.

10. A composition as set forth in claim 9 wherein said bioactive agent is a chemotherapeutic agent.

11. A composition as set forth in claim 1 wherein said lipid encapsulated emulsion has an outer coating or outer monolayer composed of a material selected from the group consisting of a natural or synthetic phospholipid, a fatty acid, cholesterol, lysolipid, sphingomyelin, tocopherol, glucolipid, stearylamine, cardiolipin, a lipid with ether or ester linked fatty acids and a polymerized lipid.

12. A composition as set forth in claim 1 wherein said outer monolayer of said emulsion also contains an additional surfactant incorporated therein for stabilizing said emulsion.

13. A composition as set forth in claim 12 wherein said additional surfactant is selected from the group consisting of nonionic and amphoteric surfactants.

14. A composition as set forth in claim 12 wherein said surfactant contains a cationic lipid to facilitate adhesion of said bioactive agent to said emulsion particles.

15. A composition as set forth in claim 14 wherein said cationic lipid is selected from the group consisting of N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride, 1,2-dioleoyloxy-3-(trimethylammonio)propane, 1,2-dioleoyl-3-(4'-trimethylammonio)butanoyl-sn-glycerol, 1,2-diacyl-3-trimethylammonium-propane,1,2-diacyl-3-dimethylammonium-propane,1,2-diacyl-sn-glycerol-3-ethylphosphochloine, and 3β-[N',N'-dimethylaminoethane)-carbamol]cholesterol-HCl.

16. A composition as set forth in claim 1 wherein said emulsion contains an emulsifying and/or solubilizing agent.

17. A composition as set forth in claim 1 wherein said emulsion particles have a diameter in the range of approximately 0.01 to 10 microns.

18. A composition as set forth in claim 17 wherein said emulsion particles have a diameter in the range of approximately 0.1 to 0.5 microns.

19. A composition as set forth in claim 1 wherein said emulsion contains a primer material incorporated into the outer monolayer thereof to covalently bond said ligand with said emulsion.

20. A composition as set forth in claim 19 wherein said primer material is selected from the group consisting of 1-ethyl-3-(3-N-N-dimethylaminopropyl)carbodiimide hydrochloride, 1-cyclohexyl-3-(2-morpholinoethyl)carbodimide methyl-p-toluenesulfonate, phosphatidylethanolamine, N-caproylamine phosphatidylethanolamine, N-dodecanylamine phosphatidylethanolamine, phosphotidylthioethanol, 1,2-diacyl-sn-glycerol-3-phosphoethanolamine-N-[4-p-maleimidephenyl)-butyramide, N-succinyl-phosphatidylethanolamine, N-glutaryl-phosphatidylethanolamine, N-dodecanyl-phosphatidylethanolamine, N-biotinyl-phosphatidylethanolamine, N-biotinylcaproyl-phosphatidylethanolamine, and phosphatidylethylene glycol.

21. A composition as set forth in claim 1 wherein said ligand is conjugated directly to said emulsion by direct adsorption of said ligand to the oil/aqueous interface of said emulsion.

22. A composition for use in delivering a bioactive agent to targeted tissues or cells comprising:

(a) a lipid encapsulated oil in water emulsion; and

(b) a combination site-specific targeting ligand/bioactive agent in or on the surface of the outer monolayer of said emulsion; said combination ligand/bioactive agent being conjugated directly or indirectly to said emulsion and said composition providing facilitated delivery of said bioactive agent through prolonged association and increased

contact of the ligand-bound, lipid encapsulated emulsion particles with the lipid bilayer of said target tissues or cells.

23. A composition as set forth in claim 22 wherein said combination ligand/bioactive agent is selected from the group consisting of antibodies, peptide fragments and mimetics.

24. A composition as set forth in claim 23 wherein said combination ligand/bioactive agent is an antibody.

25. A composition as set forth in claim 22 wherein said oil in water emulsion contains a fluorochemical.

26. A composition as set forth in claim 25 wherein said fluorochemical is a fluorocarbon.

27. A composition as set forth in claim 25 wherein said fluorochemical is a liquid with a boiling point above approximately 30°C.

28. A composition as set forth in claim 27 wherein said fluorochemical liquid has a boiling point above approximately 90°C.

29. A composition as set forth in claim 22 wherein said lipid encapsulated emulsion has an outer coating or outer monolayer composed of a material selected form the group consisting of a natural or synthetic phospholipid, a fatty acid, cholesterol, lysolipid, sphingomyelin, tocopherol, glucolipid, stearylamine, cardiolipin, a lipid with ether or ester linked fatty acids and a polymerized lipid.

30. A composition as set forth in claim 22 wherein said outer monolayer of said emulsion also contains an additional surfactant incorporated therein for stabilizing said emulsion.

31. A composition as set forth in claim 30 wherein said surfactant contains a cationic lipid to facilitate adhesion of said ligand/bioactive agent to said emulsion particles.

32. A composition as set forth in claim 22 wherein said emulsion contains an emulsifying agent and/or solubilizing agent.

33. A composition as set forth in claim 27 wherein said emulsion particles have a diameter in the range of approximately 0.01 to 10 microns.

34. A composition as set forth in claim 33 wherein said emulsion particles have a diameter in the range of approximately 0.1 to 0.5 microns.

35. A composition as set forth in claim 22 wherein said emulsion contains a primer material incorporated into the outer lipid monolayer thereof to covalently bond said ligand/bioactive agent with said emulsion.

36. A composition as set forth in claim 22 wherein said ligand/bioactive agent is conjugated directly to said emulsion by direct adsorption of the ligand/bioactive agent to the oil/aqueous interface of said emulsion.

37. A method for improved delivery of a bioactive agent to targeted tissues or cells comprising administering to said tissues or cells a composition comprising:

(a) a site-specific targeting ligand;

(b) a lipid encapsulated oil in water emulsion; and

(c) a bioactive agent in or on the surface of the outer monolayer of said emulsion; said ligand being conjugated directly or indirectly to said emulsion; whereby said composition provides facilitated delivery of said bioactive agent through prolonged association and increased contact of the ligand-bound, lipid encapsulated emulsion particles with the lipid bilayer of said target tissues or cells.

38. A method as set forth in claim 37 wherein said site-specific targeting ligand is selected from the group consisting of antibodies, antibody fragments, peptides, asialoglycoproteins, polysaccharides, aptamers, small molecules, nucleic acids, peptidomimetics, mimetics and drugs.

39. A method as set forth in claim 38 wherein said site-specific targeting ligand is an antibody.

40. A method as set forth in claim 37 wherein said oil in water emulsion contains a fluorochemical.

41. A method as set forth in claim 40 wherein said fluorochemical is a fluorocarbon.

42. A method as set forth in claim 41 wherein said fluorocarbon is perfluorooctylbromide.

43. A method as set forth in claim 40 wherein said fluorochemical is a liquid with a boiling point above approximately 30°C.

44. A method as set forth in claim 43 wherein said fluorochemical liquid has a boiling point above approximately 90°C.

45. A method as set forth in claim 37 wherein said bioactive agent is selected from the group consisting of chemotherapeutic agents, drugs, genetic materials, nucleic acid-based therapy, protein or peptide therapy, radioactive isotopes or combinations thereof.

46. A method as set forth in claim 45 wherein said bioactive agent is a chemotherapeutic agent.

47. A method as set forth in claim 45 wherein said lipid encapsulated emulsion has an outer coating composed of a material selected from the group consisting of a natural or synthetic phospholipid, a fatty acid, cholesterol, lysolipid, sphingomyelin, tocopherol, glucolipid, stearylamine, cardiolipin, a lipid with ether or ester linked fatty acids and a polymerized lipid.

48. A method as set forth in claim 33 wherein said outer monolayer of said emulsion also contains an additional surfactant incorporated thereon for stabilizing said emulsion.

49. A method as set forth in claim 48 wherein said additional surfactant is selected from the group consisting of nonionic and amphoteric surfactants.

50. A method as set forth in claim 37 wherein said surfactant contains a cationic lipid to facilitate adhesion of said bioactive agent to said emulsion particles.

51. A method as set forth in claim 37 wherein said emulsion contains an emulsifying and/or solubilizing agent.

52. A method as set forth in claim 37 wherein said emulsion particles have a diameter in the range of approximately 0.01 to 10 microns.

53. A method as set forth in claim 52 wherein said emulsion particles have a diameter in the range of approximately 0.1 to 0.5 microns.

54. A method as set forth in claim 37 wherein said emulsion contains a primer material incorporated into the outer monolayer thereof to covalently bond said ligand with said emulsion.

55. A method as set forth in claim 37 wherein said ligand is conjugated directly to said emulsion by direct adsorption of said ligand to the oil/aqueous outerface of said emulsion.

56. A method for improved delivery of a bioactive agent to targeted tissues or cells comprising administering to said tissues or cells a composition comprising:

(a) a lipid encapsulated oil in water emulsion; and

(b) a combination site-specific targeting ligand/bioactive agent in or on the surface of the outer monolayer of said emulsion; said combination ligand/bioactive agent being conjugated directly or indirectly to said emulsion and said composition providing facilitate delivery of said bioactive agent through prolonged association and increased contact of the ligand-bound, lipid encapsulated emulsion particles with the lipid bilayer of said target tissues or cells.

57. A method as set forth in claim 50 wherein said combination ligand/bioactive agent is selected from the group consisting of antibodies, antibody fragments, peptides, asialoglycoproteins, polysaccharides, aptamers, small molecules, nucleic acids, peptidomimetics, mimetics and drugs.

58. A method as set forth in claim 57 wherein said combination ligand/bioactive agent is an antibody.

59. A method as set forth in claim 56 wherein said oil in water emulsion contains a fluorochemical.

60. A method as set forth in claim 59 wherein said fluorochemical is a fluorocarbon.

61. A method as set forth in claim 59 wherein said fluorochemical is a liquid with a boiling point above approximately 30°C.

62. A method as set forth in claim 61 wherein said fluorochemical liquid has a boiling point above approximately 90°C.

63. A method as set forth in claim 56 wherein said lipid encapsulated emulsion has an outer coating or outer monolayer composed of a material selected from the group consisting of a natural or synthetic phospholipid, a fatty acid, cholesterol, lipolipid, sphengomyelin, tocopheral, glucolipid, stearylamine, cardiolipin, a lipid with ether or ester linked fatty acids and a polymerized lipid.

64. A method as set forth in claim 56 wherein said outer monolayer of said emulsion also contains an additional surfactant incorporated therein for stabilizing said emulsion.

65. A method as set forth in claim 64 wherein said surfactant contains a cationic lipid to facilitate adhesion of said ligand/bioactive agent to said emulsion particles.

66. A method as set forth in claim 56 wherein said emulsion contains an emulsifying agent and/or solubilizing agent.

67. A method as set forth in claim 56 wherein said emulsion particles have a diameter in the range of approximately 0.01 to 10 microns.

68. A method as set forth in claim 67 wherein said emulsion particles have a diameter in the range of approximately 0.1 to 0.5 microns.

69. A method as set forth in claim 56 wherein said emulsion contains a primer material incorporated into the outer lipid monolayer thereof to covalently bond said ligand/bioactive agent with said emulsion.

70. A method as set forth in claim 56 wherein said ligand/bioactive agent is conjugated directly to said emulsion by direct adsorption of the ligand/bioactive agent to the oil/aqueous interface of said emulsion.